REMARKS

Claims 1-6, 8-16, 18-25, 27-28 and 33 were pending and claims 1-6, 8-16, 18-25, 27-28 and 33 were variously rejected under 35 U.S.C. § 112, first paragraph.

By this amendment, claims 1, 10 and 20 have been amended and new claims 36-39 have been added without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, *inter alia*, throughout the specification, for example, at page 22, lines 1-3. Support for new claims 36-39 is found, *inter alia*, at page 17, line 23.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicant has carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Examiner Interview

Applicant thanks Examiners Sullivan and Ketter for participating in an interview on September 25, 2003 regarding the outstanding rejections in this application. Applicant also thanks Examiner Sullivan for faxing a copy of his Interview Summary (PTOL-413) on October 16, 2003. The topics discussed in the interview and the interview summary are reflected herein.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1-6, 8-16, 18-25, 27-28 and 33 were rejected under 35 U.S.C. §112, first paragraph, for allegedly not being enabled. Applicant respectfully traverses this rejection.

The amended claims are directed to methods of preventing a symptom, reducing severity, and reducing recurrence of a symptom of herpes simplex virus infection in a mammal comprising administering an ISS-containing polynucleotide composition in the absence of administration of a herpes simplex virus antigen. In the claims, the ISS comprises the sequence 5'-C, G-3' and the polynucleotide is less than about 200 nucleotides in length and comprises a phosphate backbone. The claims are also directed to a kit for use in ameliorating or preventing a symptom of herpes virus infection comprising a composition comprising a polynucleotide comprising particular ISS sequences and instructions for use, wherein the kit does not comprise a herpes simplex virus antigen.

The Examiner finds that "the claims lack enablement for immunostimulatory sequences other than those set forth as SEQ ID NO:1 and 9 to and [sic] mammals other than mice and guinea pigs." Office Action, page 3. In support of this conclusion, the Examiner states that "the art is immature and the factors dictating efficacy of CpG-containing oligonucleotides in mammals are largely unknown." The Examiner further asserts that "in order to practice the claimed invention according to its full scope, the skilled artisan would have to identify, by blind trial and error experimentation, an immunostimulatory oligonucleotide capable of eliciting an immune response of sufficient magnitude to prevent a symptom of herpes infection in each of the approximately 5000 species encompassed by the claim." Office Action, page 6. In the Interview Summary, the Examiners acknowledge "that the animal models used in the reduction to practice are valid models for HSV infection" but state that "the models presented do not accurately predict the effects of immunostimulatory oligonucleotides across mammalian species." Interview Summary, page 3. Applicant respectfully disagrees with this position.

Applicant submits that the specification provides adequate guidance to enable one skilled in the art to make and use the claimed invention. Many examples of ISS for use in the invention and methods for their synthesis are provided, for example, on pages 24-34. Examples of administration regimens are provided, for example, on pages 34-35. Examples of formulations are provided, for

example, on pages 35-36. Examples of dosage ranges of ISS-containing polynucleotides for use in the claimed methods are provided, for example, on page 36. Examples of means of administration are provided, for example, on pages 37-38. Means of assessing the functional activity of the ISS-containing polynucleotides as claimed are provided, for example, on pages 38-40. The working examples in the specification (pages 42-48) exemplify ISS-containing polynucleotides with activity as claimed. Applicant maintains that such extensive disclosure provides adequate guidance such that a skilled artisan would be able to practice the invention without undue experimentation.

With regard to the state of the art, Applicant respectfully notes that polynucleotides with immunostimulatory sequences active in cells of many mammalian species have been described in scientific literature, including human, monkeys, chimpanzees, cows, swine, dogs, cats, rabbits, mice and rats. In particular, much has been described about ISS activity in human cells and immunostimulatory sequences active in human cells have been the subject of much scientific and patent literature. Thus, Applicant concurs with the Examiner's assessment of the relative level of skill in the art as "high" (Office Action, page 6) but submits that the ISS art is more mature than the Examiner asserts.

Applicant respectfully notes that the test for enablement is not whether a certain amount of experimentation is required to practice an invention, but rather whether the amount of experimentation is "undue." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Applicant respectfully submits that the specification has provided a reasonable amount of guidance to the skilled artisan with respect to the direction in which the experimentation should proceed and that the skilled artisan would be able to extend the teachings of the specification and the art to other mammals.

In addition, as discussed during the Examiner Interview, the Office has recently issued claims directed to methods of treating a mammal, a subject or an individual through administering an immunostimulatory or immunomodulatory polynucleotide comprising an ISS, wherein the ISS

comprises the sequence 5'-C, G-3'.[1] In claims which recite "individual" or "subject", the terms are defined in the patents as including mammals. All of these patents have claimed priority dates earlier than or within weeks of the priority date of the instant application.

The claims in these patents are supported with experiments in which a limited number of 5'-C, G-3' containing oligonucleotides were tested for a particular activity or effect in a mouse model and, in some cases, on human cells in culture. Thus, in these cases, the Office has apparently deemed the state of the art such that the task of identifying nucleotides surrounding the core 5'-C, G-3' motif for a given mammal as not an undue burden to the skilled artisan.

As presented in the response to the Office Action filed March 24, 2003, the court in *In re Wands* found that the enablement requirement was satisfied by a "disclosure [that] provides considerable direction and guidance on how to practice [the] invention and presents working examples," in view of the fact that "[t]here was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *Id.* at 740. As outlined herein, the specification provides considerable guidance as to how to identify and make ISS-containing polynucleotides for use in the invention and how to assess the activity of ISS-containing polynucleotides in the claimed methods. Thus, Applicant maintains that, following the reasoning in the *In re Wands* decision, the disclosure is adequate to enable the invention as claimed.

Applicant respectfully submits that the specification provides adequate guidance pertaining how to make and use the claimed immunomodulatory polynucleotides. Thus, the pending claims are in compliance with the enablement requirements.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

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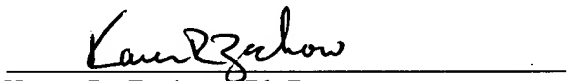
[1] See, for example, U.S. Pat. Nos. 6,613,751, 6,552,006, 6,534,062 and 6,498,148, submitted herewith.

CONCLUSION

Applicant believes that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicant's representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882001100. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: October 17, 2003 By: 

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